rewritten in independent form. Applicants further request reconsideration of the subject application based on the instant amendments and following remarks.

Claims 3, 9, 10, 13, 15, 17, 19, and 20 have been amended. No new matter has been added by the claim amendments. Support for the amendment to claims can be found in the claims as originally filed and throughout the specification.

Claims 3, 9, 10, 13-15, 17, 19, and 20 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Although applicants respectfully disagree with the position taken by the Examiner, the claims have been amended to provide for "(cycloalkyl)alkyl" groups having between 4 and 11 carbon atoms. Applicants believe that the range of 4 to 11 carbon atoms is fully supported by the specification including the repeated recitation of C_{3-7}cycloalkylC_{1-4}alkyl groups.

Claims 3, 5-21, and 23 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner has rejected claims 2 and 3 as indefinite for reciting several double inclusions.

The rejection is traversed.

Applicants note that MPEP 2173.05(o) addresses Double Inclusion in a claim. This section of the MPEP provides that "there is no *per se* rule that 'double inclusion' is improper in a claim." MPEP 2173.05(o), second paragraph, further provides:

> The mere fact that a compound may be embraced by more than one member of a Markush group recited in the claim does not lead to any uncertainty as to the scope of that claim for either examination or infringement purposes. On the other hand, where a claim directed to a device can be read to include the same element twice, the claim may be indefinite.

Applicants note that each substituent included within the variable X which is merely embraced by two members of the Markush group recited for variable X in claims 3 and 9. As provided by MPEP 2173(o), the mere presence of multiple recitations of a chemical substituent within a Markush group does not render the claim indefinite for examination purposes. Thus, claims 3 and 9 are clear and definite. Claims 5 through 8 and claims 10-21 and 23 depend from either claim 3 or claim 9 and are therefore also definite.

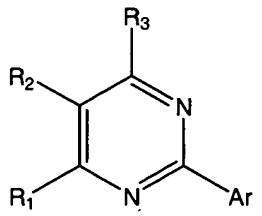
Claims 3, 5-21, and 23 are fully compliant with the requirements of 35 U.S.C. §112, including the requirements of the first and second paragraph. Thus, Applicants respectfully request that the rejections be withdrawn.

Claims 1 and 2 were rejected under 103(a) as being unpatentable over Murata et al. (U.S. Patent 5,972,946).

The Examiner indicated at page 2, lines 2-5 of the Office Action dated January 29, 2003 that a newly found reference, i.e., the Murata reference (U.S. Patent 5,972,946), is the basis for the present rejection under §103(a).

The rejection is respectfully traversed.

The present invention provides in claims 1 and 2 compounds of the following formula:



wherein **the 4-ring position and the 6-ring position (i.e., R_4 and R_6) are not chloro**, and wherein the 5-ring position (i.e. R_2) is optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted alkoxy, optionally substituted aminoalkyl, optionally substituted mono or dialkylamino, optionally substituted alkylthio, optionally substituted alkylsulfinyl, optionally substituted alkylsulfonyl, optionally substituted mono or dialkylcarboxamide, optionally substituted carbocyclic aryl or optionally substituted heteroaryl having from 1 to 3 rings, and 3 to 8 ring members in each ring and 1 to about 3 heteroatoms

In contrast, Murata recites certain compounds that have a 2-phenyl-**4-chloro**-pyrimidine structure, which at the 4 and optionally at the 6 position is substituted with one or two chloro groups, as intermediates in the preparation of a family of acetamide derivatives according to Formula I. See, the abstract and Table 11 at column 29 of the Murata document.

Murata does not contain any suggestion that modification of the 4-chloro-substituted pyrimidines would possess any utility or desirable properties. Moreover, one skilled in the art would not be motivated to prepare analogs of the 4-chloro-substituted pyrimidines because the disclosed compounds 22-30 are easy to make and carry forward in the synthetic procedure provided by Murata.

Motivation is an important element in a determination of obviousness. As the Court of Appeals for the Federal Circuit has stated:

> In determining whether a case of *prima facie* obviousness exists, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification.

In re Lalu, 223 USPQ 1257, 1258 (CAFC (Fed. Cir. 1984)), citing *In re Taborsky*, 502 F.2d 775, 780, 183 USPQ 50, 55 (CCPA 1974).

> How can there be obviousness of structure, or particularly of the subject matter as a whole, when no apparent purpose or result is to be achieved, no reason or motivation to be satisfied, upon modifying the reference compounds structure? Where the prior art reference neither discloses nor suggests a utility for certain described compounds, why should it be said that a reference makes obvious to one of ordinary skill in the art an isomer, homolog or analog of related structure, when that mythical, but intensely practical, person knows of no "practical" reason to make the reference compounds, much less any structurally related compounds?

In re Lalu, 223 USPQ 1257, 1259 (CAFC (Fed. Cir. 1984)), citing *In re Stemniski*, 444 F.2d 581, 586, 170 USPQ 343, 347 (CCPA 1971).

Murata provides a functional synthetic procedure for the preparation of the acetamide derivatives of Formula I which makes use of a series of 4-chloro-pyrimidine intermediates, e.g., compounds 22-30. One of ordinary skill in the art would have had no motivation based on the Murata disclosure to make analogs of any of the intermediate compounds disclosed therein. More particularly, one of ordinary skill in the art would not have been motivated to prepare other 4-halo pyrimidine compounds analogous to those of compounds 22-30 merely because other halogen atoms have similar leaving group activity to chloro substituted compounds. Compounds 22-30 are easy to make and are readily transformed into the acetamide derivatives which are recited in Examples 1-63 on column 35-37 of Murata.

One of ordinary skill in the art would not have been motivated to investigate alternate leaving groups in a literature synthesis, particularly where the alternate leaving groups are more costly to prepare, in the absence of an expected benefit to such investigation. The Examiner has

not set forth any reasonable benefit which would motivate a skilled artisan to investigate non-chloro halogen analogs of compounds 22-30. Moreover, the increased cost or additional experimentation associated with the preparation of non-chloro analogs suggests that such investigation would be impractical based on the disclosure of Murata.

Thus, the compounds provided by claims 1 and 2 of the instant invention would not have been obvious based on the disclosure of structurally related synthetic intermediates by Murata. Therefore claims 1 and 2 are patentable over the disclosure of Murata.

In view thereof, reconsideration and withdrawal of the rejection are requested.

Applicants believe that additional fees are not required for consideration of the within Response. However, if for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,

Date: April 18, 2003 By: _____
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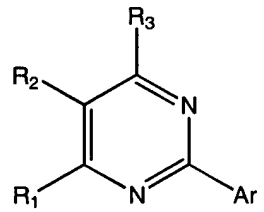
VERSION WITH CHANGES MARKED

(Additions are underlined; deletions are bracketed.)

IN THE CLAIMS

Kindly amend claims 3, 9, 10, 13, 15, 17, 19, and 20, as follows:

3. (thrice amended) A compound of the formula



or a pharmaceutically acceptable salt thereof, wherein:

R_1 and R_3 are independently selected from hydrogen, halogen, cyano, C_{1-6} alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, (C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, (C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, -O(C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, -O(C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, -O(C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, halo(C_{1-6})alkyl, haloC_{2-6}alkenyl, haloC_{2-6}alkynyl, -O(halo(C_{1-6})alkyl), -O(halo(C_{2-6})alkenyl), -O(halo(C_{2-6})alkynyl), -O(C_{1-6}alkyl), -O(C_{2-6}alkenyl), -O(C_{2-6}alkynyl), S(O)$_n$(C_{1-6}alkyl, S(O)$_n$(C_{2-6}alkenyl), and S(O)$_n$(C_{2-6}alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted with one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

and

where each C_{3-7}cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

with the proviso that not both R_1 and R_3 are hydrogen;

R_2 is selected from the group consisting of $-XR_A$ and Y; and

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, pyridizinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, cyano, amino, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), -NHC(=O)(C_{1-6}alkyl), -N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl), -NHS(O)$_n$(C_{1-6}alkyl), -S(O)$_n$(C_{1-6} alkyl), -S(O)$_n$NH(C_{1-6}alkyl), -S(O)$_n$N(C_{1-6} alkyl)(C_{1-6}alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_D, C_{2-6} alkenyl substituted with 0-2 R_D, C_{2-6}alkynyl substituted with 0-2 R_D, C_{3-7}cycloalkyl substituted with 0-2 R_D, (C_{3-7}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_D, C_{1-6}alkoxy substituted with 0-2 R_D, -NH(C_{1-6}alkyl) substituted with 0-2 R_D, -N(C_{1-6}alkyl)(C_{1-6}alkyl) each C_{1-6}alkyl independently substituted with 0-2 R_D, $-XR_A$, and Y;

R_D is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -S(O)$_n$(alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl)(C_{1-4}alkyl), $-XR_A$, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -S(O)$_n$NH-, -S(O)$_n$$NR_B$-, -OC(=S)S-, -NHC(=O)-, -NR_BC(=O)-, -NHS(O)$_n$-, -OSiH_n(C_{1-4}alkyl)$_{2-n}$-, and $-NR_BS(O)_n$-;

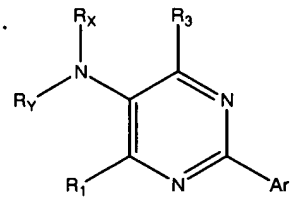
Y and Z are independently selected at each occurrence from: 3- to 7-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy,

amino, cyano, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl),and -$S(O)_n$(alkyl),

said 3- to 7-memberered heterocyclic groups containing one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen; and

n is independently selected at each occurrence from 0, 1, and 2.

9. (thrice amended) A compound of Formula A



Formula A

or a pharmaceutically acceptable salt thereof, wherein:

R_X and R_Y are the same or different and are independently selected from:

a) hydrogen,

b) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, cycloalkyl(alkyl) groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:

i) hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen,

halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), and -$S(O)_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

R_1 and R_3 are independently selected from hydrogen, halogen, cyano, C_{1-6} alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, (C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, (C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, -O(C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, -O(C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, -O(C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, halo(C_{1-6})alkyl, haloC_{2-6}alkenyl, haloC_{2-6}alkynyl, -O(halo(C_{1-6})alkyl), -O(halo(C_{2-6})alkenyl), -O(halo(C_{2-6})alkynyl), -O(C_{1-6}alkyl), -O(C_{2-6}alkenyl), -O(C_{2-6}alkynyl), $S(O)_n$(C_{1-6}alkyl), $S(O)_n$(C_{2-6}alkenyl), and $S(O)_n$(C_{2-6}alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

and

where said C_{3-7}cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino

with the proviso that not both R_1 and R_3 are hydrogen;

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with

one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), -NHC(=O)(C_{1-6}alkyl), -N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl), -NHS(O)$_n$(C_{1-6}alkyl), -S(O)$_n$(C_{1-6} alkyl), -S(O)$_n$NH(C_{1-6}alkyl), -S(O)$_n$N(C_{1-6} alkyl)(C_{1-6}alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, and C_{1-6}alkyl substituted with 0-2 R_D, C_{2-6} alkenyl substituted with 0-2 R_D, C_{2-6}alkynyl substituted with 0-2 R_D, C_{3-7}cycloalkyl substituted with 0-2 R_D, (C_{3-7}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_D, C_{1-6}alkoxy substituted with 0-2 R_D, -NH(C_{1-6}alkyl) substituted with 0-2 R_D, -N(C_{1-6}alkyl)(C_{1-6}alkyl) each C_{1-4}alkyl independently substituted with 0-2 R_D, -XR_A, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimdine ring shown in Formula A is substituted;

R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -S(O)$_n$(alkyl) halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl)(C_{1-4}alkyl), -XR_A, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -S(O)$_n$NH-, -S(O)$_n$$NR_B$-, -OC(=S)S-, -NHC(=O)-, -NR_BC(=O)-, -NHS(O)$_n$-, -OSiH_n(C_{1-4}-alkyl)$_{2-n}$[)]-, and –NR_BS(O)$_n$-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl); and

n is 0, 1, or 2.

10. (thrice amended) A compound or salt according to Claim 9, wherein:

R_X and R_Y are the same or different and are independently selected from:

a) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

b) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 12carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:

i) hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

R_1 and R_3 are independently selected from hydrogen, halogen, cyano, C_{1-6} alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, (C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, (C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, -O(C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, -O(C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, -O(C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, halo(C_{1-6})alkyl, haloC_{2-6}alkenyl, haloC_{2-6}alkynyl, -O(halo(C_{1-6})alkyl), -O(halo(C_{2-6})alkenyl), -O(halo(C_{2-6})alkynyl), -O(C_{1-6}alkyl), -O(C_{2-6}alkenyl), and -O(C_{2-6}alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

and

where said C_{3-7}cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino

Ar is phenyl, which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), -NHC(=O)(C_{1-6}alkyl), -N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, and C_{1-6}alkyl substituted with 0-2 R_D, C_{2-6} alkenyl substituted with 0-2 R_D, C_{2-6}alkynyl substituted with 0-2 R_D, C_{3-7}cycloalkyl substituted with 0-2 R_D, (C_{3-7}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_D, C_{1-6}alkoxy substituted with 0-2 R_D, -NH(C_{1-6}alkyl) substituted with 0-2 R_D, -N(C_{1-6}alkyl)(C_{1-6}alkyl) each C_{1-4}alkyl independently substituted with 0-2 R_D, -XR_A, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl)(C_{1-4}alkyl), -XR_A, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -NHC(=O)-, and -NR_BC(=O)-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or

aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -N(C_{1-4}alkyl)(C_{1-4}alkyl); and

n is 0,1, or 2.

13. (thrice amended) A compound or salt according to claim 9, wherein:

Ar is phenyl mono-, di-, or tri-substituted with R_C,

R_X and R_Y, which may be the same or different, are independently selected at each occurrence from

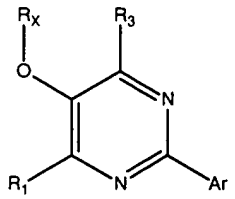
straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms; and

R_1 and R_3 are independently selected from the group consisting of hydrogen, halogen, C_{1-4}alkoxy, halo(C_{1-4})alkyl, (halo(C_{1-4})alkoxy,

C_{1-6}alkyl, which C_{1-6}alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

(C_{3-7}cycloalkyl)C_{1-4}alkyl, which (C_{3-7}cycloalkyl)C_{1-4}alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino.

15. (thrice amended) A compound or salt according to the formula



wherein:

R_X is chosen from

straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:

(a) hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and

(b) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substitutents selected from halogen, halo(C_{1-4})alkyl, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) selected from N, O, and S, with the point of attachment being either carbon or nitrogen;

R_1 and R_3 are independently selected from hydrogen, halogen, cyano, C_{1-6} alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, (C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, (C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, (C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, -O(C_{3-7}cycloalkyl$_1$)C_{1-4}alkyl, -O(C_{3-7}cycloalkyl$_1$)C_{2-4}alkenyl, -O(C_{3-7}cycloalkyl$_1$) C_{2-4}alkynyl, halo(C_{1-6})alkyl, haloC_{2-6}alkenyl, haloC_{2-6}alkynyl, -O(halo(C_{1-6})alkyl), -O(halo(C_{2-6})alkenyl), -O(halo(C_{2-6})alkynyl), -O(C_{1-6}alkyl), -O(C_{2-6}alkenyl), -O(C_{2-6}alkynyl), S(O)$_n$(C_{1-6}alkyl), S(O)$_n$(C_{2-6}alkenyl), and S(O)$_n$(C_{2-6}alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino,

and

where said C_{3-7}cycloalkyl$_1$ is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C_{1-4}alkoxy, amino, and mono- or di(C_{1-4})alkylamino

with the proviso that not both R_1 and R_3 are hydrogen;

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R_C;

R_A and R_B, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), -NHC(=O)(C_{1-6}alkyl), -N(C_{1-6}alkyl)C(=O)(C_{1-6}alkyl), -NHS(O)$_n$(C_{1-6}alkyl), -S(O)$_n$(C_{1-6} alkyl), -S(O)$_n$NH(C_{1-6}alkyl), -S(O)$_n$N(C_{1-6} alkyl)(C_{1-6}alkyl), and Z;

R_C is independently selected at each occurrence from halogen, cyano, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, and C_{1-6}alkyl substituted with 0-2 R_D, C_{2-6} alkenyl substituted with 0-2 R_D, C_{2-6}alkynyl substituted with 0-2 R_D, C_{3-7}cycloalkyl substituted with 0-2 R_D, (C_{3-7}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_D, C_{1-6}alkoxy substituted with 0-2 R_D, -NH(C_{1-6}alkyl) substituted with 0-2 R_D, -N(C_{1-6}alkyl)(C_{1-6}alkyl) each C_{1-4}alkyl independently substituted with 0-2 R_D, -XR_A, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimdine ring shown in Formula A is substituted;

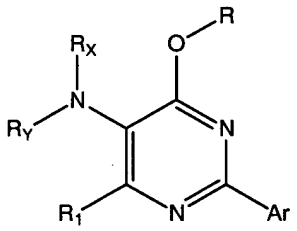
R_D is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -S(O)$_n$(alkyl) halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-4}alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl)(C_{1-4}alkyl), -XR_A, and Y;

X is independently selected at each occurrence from the group consisting of -CH_2-, -CHR_B-, -O-, -C(=O)-, -C(=O)O-, -S(O)$_n$-, -NH-, -NR_B-, -C(=O)NH-, -C(=O)NR_B-, -S(O)$_n$NH-, -S(O)$_n$$NR_B$-, -OC(=S)S-, -NHC(=O)-, -NR_BC(=O)-, -NHS(O)$_n$-, -OSiH_n(C_{1-4}-alkyl$_{2-n}$)-, and –NR_BS(O)$_n$-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl); and

n is 0, 1, or 2.

17. (thrice amended) A compound or salt according to Claim 3 of Formula B:



FORMULA B

Ar is phenyl mono-, di-, or tri-substituted with R_C;

R is selected from straight, branched, or cyclic alkyl groups, (cycloalkyl)alkyl groups, straight, branched, or cyclic alkenyl groups, or straight or branched alkynyl groups, and which are optionally substituted by one or more substituents independently chosen from oxo, hydroxy, halogen, cyano, -O(C_{1-4} alkyl), amino, -NH(C_{1-4} alkyl), and -N(C_{1-4} alkyl)(C_{1-4} alkyl);

R_1 is selected from hydrogen, halogen, cyano, C_{1-4} alkyl, (C_{3-7}cycloalkyl)C_{1-4}alkyl, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, and -O(C_{1-4}alkyl); and

R_X and R_Y are the same or different and are independently selected from:

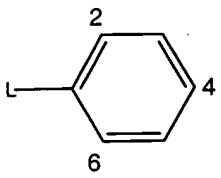
a) hydrogen,

b) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may

be further substituted with one or more substituent(s) independently selected from (i)hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl), and (ii)3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substitutents selected from halogen, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), –N(C_{1-4}alkyl)(C_{1-4}alkyl), and -S(O)$_n$(alkyl), wherein said 3- to 7-memberered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

19. (thrice amended) A compound or salt according to Claim 17, wherein Ar is a phenyl group of the formula:



wherein L indicates a bond to the pyrimidine ring in Formula B
and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

i) halogen, cyano, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6}alkoxy, (C_{1-4}alkoxy)C_{1-4}alkoxy, and mono- or di(C_{1-4}alkyl)amino,

ii) C_{1-6} alkyl and C_{1-6}alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -N(C_{1-4}alkyl)(C_{1-4}alkyl);

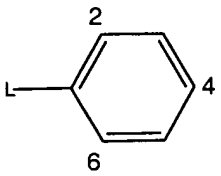
R_X and R_Y are the same or different and are independently selected from the group consisting of:

a) hydrogen (with the proviso that R_x and R_Y are not both hydrogen),

b) -(C=O)alkyl$_A$, wherein alkyl$_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, which may be further substituted with one or more substituent(s) independently selected from hydroxy, halogen, amino, cyano, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -NH(C_{1-4}alkyl)(C_{1-4}alkyl).

20. (thrice amended) A compound or salt according to Claim 17, wherein Ar is a phenyl group of the formula:



wherein L indicates a bond to the pyrimidine ring in Formula B
and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

i) halogen, cyano, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6}alkoxy, (C_{1-4}alkoxy)C_{1-4}alkoxy, and mono- or di(C_{1-4}alkyl)amino,

ii) C_{1-6} alkyl and C_{1-6}alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C_{1-4}alkyl, -O(C_{1-4}alkyl), -NH(C_{1-4}alkyl), and -N(C_{1-4}alkyl)(C_{1-4}alkyl);

R_X and R_Y are the same or different and are independently selected from the group consisting of:

a) hydrogen (with the proviso that R_x and R_Y are not both hydrogen),

b) -(C=O)$alkyl_A$, wherein $alkyl_A$ is a straight or branched alkyl group having from 1 to 8 carbon atoms;

c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to [12]11 carbon atoms, straight, branched, or

cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms.